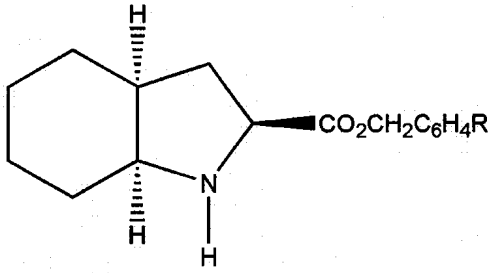
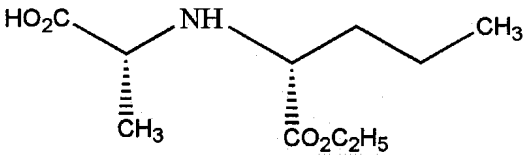
AMENDMENTS TO THE CLAIMS

Listing of Claims:

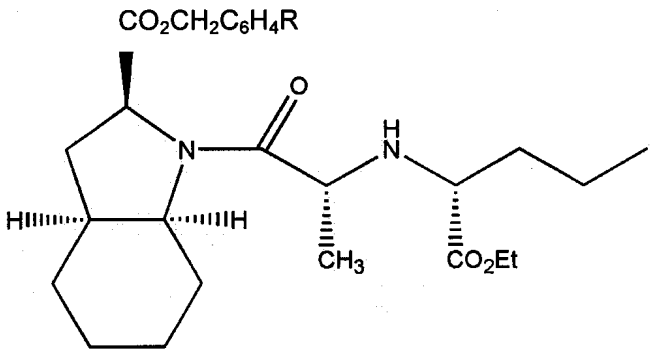
1. (Original) A process for preparing perindopril, or a pharmaceutically acceptable salt thereof, which process comprises coupling a substituted benzyl ester of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid (I) with N-[(S)-carbethoxybutyl]-(S)-alanine (II):



I



II



III

where R represents a halo, C_{1-4}alkoxy or nitro substituent, to form the ester of formula III, wherein the coupling is carried out in the presence of N,N-dicyclohexyl carbodiimide (DCC) and

1-hydroxybenzotriazole (HOBT): and converting the ester of formula III to perindopril or a pharmaceutically acceptable salt thereof.

2-35. (Canceled)

36. (New) The process according to claim 1, wherein R represents a 4-substituent.

37. (New) The process according to claim 1, wherein the coupling is carried out at a temperature below 20°C, preferably in the range 10-15°C.

38. (New) The process according to claim 1, wherein from 1.5 to 1.7 mole DCC are employed per mole of the ester of formula I.

39. (New) The process according to claim 1, which includes deprotection the compound of formula III by hydrogenolysis in the presence of a noble metal catalyst.

40. (New) The process according to claim 39, wherein the catalyst is palladium on carbon.

41. (New) The process according to claim 1, wherein the perindopril is converted to a pharmaceutically acceptable salt.

42. (New) The process according to claim 41, wherein the perindopril is converted to the tert butyl amine salt.

43. (New) A process for preparing perindopril, or a pharmaceutically acceptable salt thereof, which includes an intermediate process step wherein an aralkyl ester of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid is prepared by reaction of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid with an aralkyl alcohol, wherein either said (2S,3aS,7aS)-octahydroindole-2-carboxylic acid is treated with an excess of the alcohol and thionyl chloride, excess alcohol is distilled off and the residue treated with a solvent to obtain the aralykyl ester of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid as a hydrochloride; or said (2S,3aS,7aS)-octahydroindole-2-carboxylic acid is treated with an excess of the alcohol and heated with toluene using a molar

quantity p-toluene sulphonic acid, to obtain the aralkyl ester of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid as a salt, and converting the salt to the base, preferably by treatment with ammonia.

44. (New) The process according to claim 43, wherein the aralkyl alcohol has a substituent in the aryl group.

45. (New) The process according to claim 44, wherein the aryl group has a halo, alkoxy or nitro substituent.

46. (New) The process according to claim 45, wherein the aryl group has a 4-chloro, 4 C_{1-4}-alkoxy or 4-nitro group, substituent.

47. (New) The process according to claim 43, wherein the aralkyl group is a benzyl group or a substituted benzyl group.

48. (New) The process according to claim 1, wherein the compound of formula I has been made by an intermediate process step wherein an aralkyl ester of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid is prepared by reaction of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid with an aralkyl alcohol, wherein either said (2S,3aS,7aS)-octahydroindole-2-carboxylic acid is treated with an excess of the alcohol and thionyl chloride, excess alcohol is distilled off and the residue treated with a solvent to obtain the aralykyl ester of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid as a hydrochloride; or said (2S,3aS,7aS)-octahydroindole-2-carboxylic acid is treated with an excess of the alcohol and heated with toluene using a molar quantity p-toluene sulphonic acid, to obtain the aralkyl ester of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid as a salt, and converting the salt to the base, preferably by treatment with ammonia.

49. (New) A process for preparing perindopril, or a pharmaceutically acceptable salt thereof, which includes an intermediate process step which comprises conversion of an alkali metal salt

of S-indoline-2-carboxylic acid to (2S,3aS,7aS)-octahydroindole-2-carboxylic acid by hydrogenation at a pressure of from 5 to 20 bar.

50. (New) The process according to claim 49, wherein the hydrogenation is carried out at a pressure of 10 to 15 bar.

51. (New) The process according to claim 49, wherein said hydrogenation is effected in the presence of alkali and the octahydroindole-2-carboxylic acid salt so formed is treated with mineral acid to release the free acid.

52. (New) The process according to claim 49, wherein the alkali metal salt of said S-indoline-2-carboxylic acid is the sodium salt.

53. (New) The process according to claim 49, wherein the hydrogenation is carried out in a polar solvent selected from C_{1-4} alcohols and water, or mixtures thereof.

54. (New) The process according to claim 49, wherein the product is crystallized from acetonitrile.

55. (New) The process according to claim 49, wherein said catalyst is 5% rhodium on alumina.

56. (New) The process according to claim 43, wherein the (2S,3aS,7aS)-octahydroindole-2-carboxylic acid has been made by an intermediate process step which comprises conversion of an alkali metal salt of S-indoline-2-carboxylic acid to (2S,3aS,7aS)-octahydroindole-2-carboxylic acid by hydrogenation at a pressure of from 5 to 20 bar.

57. (New) A process for preparing perindopril, or a pharmaceutically acceptable salt thereof, which includes an intermediate process step which comprises condensation of norvaline ethyl ester with pyruvic acid to yield N-[(S)-1-carbethoxybutyl]-(S)-alanine (II), wherein said condensation is carried out under catalytic hydrogenation and said catalyst and any inorganic

salts present in the reaction medium are removed by filtration to obtain a filtrate, the filtrate is concentrated and N-[(S)-1-carbethoxybutyl]-(S)-alanine is isolated by precipitation by the addition of a solvent selected from acetone, acetonitrile and ethyl acetate.

58. (New) The process according to claim 57, wherein the condensation is effected in a lower alcohol, preferably ethanol.

59. (New) The process according to claim 57, wherein said norvaline ethyl ester is included in the reaction medium as the hydrochloride salt thereof, in the presence of a base.

60. (New) The process according to claim 57, wherein said catalytic hydrogenation is carried out in a hydrogenator, in the presence of palladium on carbon as the catalyst.

61. (New) The process according to claim 60, wherein said catalyst is 10% palladium on carbon.

62. (New) The process according to claim 57, wherein said hydrogenation is carried out at a pressure in the range of 5 to 10 bar.

63. (New) The process according to claim 57, wherein the precipitation solvent for N-[(S)-1-carbethoxybutyl]-(S)-alanine is acetone.

64. (New) The process according to claim 1, wherein compound II has been made by an intermediate process step which comprises condensation of norvaline ethyl ester with pyruvic acid to yield N-[(S)-1-carbethoxybutyl]-(S)-alanine (II), wherein said condensation is carried out under catalytic hydrogenation and said catalyst and any inorganic salts present in the reaction medium are removed by filtration to obtain a filtrate, the filtrate is concentrated and N-[(S)-1-carbethoxybutyl]-(S)-alanine is isolated by precipitation by the addition of a solvent selected from acetone, acetonitrile and ethyl acetate.

65. (New) The process according to claim 43, which further comprises converting perindopril free base to perindopril erbumine.

66. (New) A process according to claim 1, wherein the compound of formula I has been made by an intermediate process step wherein an aralkyl ester of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid is prepared by reaction of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid with an aralkyl alcohol, wherein either said (2S,3aS,7aS)-octahydroindole-2-carboxylic acid is treated with an excess of the alcohol and thionyl chloride, excess alcohol is distilled off and the residue treated with a solvent to obtain the aralykyl ester of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid as a hydrochloride; or said (2S,3aS,7aS)-octahydroindole-2-carboxylic acid is treated with an excess of the alcohol and heated with toluene using a molar quantity p-toluene sulphonic acid, to obtain the aralkyl ester of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid as a salt, and converting the salt to the base, preferably by treatment with ammonia; and wherein compound II has been made by an intermediate process step which comprises condensation of norvaline ethyl ester with pyruvic acid to yield N-[(S)-1-carbethoxybutyl]-(S)-alanine (II), wherein said condensation is carried out under catalytic hydrogenation and said catalyst and any inorganic salts present in the reaction medium are removed by filtration to obtain a filtrate, the filtrate is concentrated and N-[(S)-1-carbethoxybutyl]-(S)-alanine is isolated by precipitation by the addition of a solvent selected from acetone, acetonitrile and ethyl acetate.

67. (New) The process according to claim 43, wherein the (2S,3aS,7aS)-octahydroindole-2-carboxylic acid has been made by an intermediate process step which comprises conversion of an alkali metal salt of S-indoline-2-carboxylic acid to (2S,3aS,7aS)-octahydroindole-2-carboxylic acid by hydrogenation at a pressure of from 5 to 20 bar; and wherein compound II has been made by an intermediate process step which comprises condensation of norvaline ethyl ester with

pyruvic acid to yield N-[(S)-1-carbethoxybutyl]-(S)-alanine (II), wherein said condensation is carried out under catalytic hydrogenation and said catalyst and any inorganic salts present in the reaction medium are removed by filtration to obtain a filtrate, the filtrate is concentrated and N-[(S)-1-carbethoxybutyl]-(S)-alanine is isolated by precipitation by the addition of a solvent selected from acetone, acetonitrile and ethyl acetate.